

WHAT IS CLAIMED:

1. A conjugate comprising poly-D-gamma glutamic acid covalently linked to an immunogenic carrier protein wherein the poly-D-gamma glutamic acid is above about 100 kDa.

2. A conjugate comprising poly-D-gamma glutamic acid covalently linked to an immunogenic carrier protein wherein the poly-D-gamma glutamic acid is above about 200 kDa.

3. A conjugate comprising poly-D-gamma glutamic acid covalently linked to an immunogenic carrier protein wherein the poly-D-gamma glutamic acid is above about 300 kDa.

4. The conjugate according to any of claims 1-3 wherein the poly-D-gamma-glutamic acid is covalently linked to the carrier protein by N-(epsilon-maleimidocaproic acid)hydrazide.

5. The conjugate according to any of claims 1-3 wherein the carrier protein is selected from the group consisting of outer membrane protein complex (OMPC) of *Neisseria meningitidis*, tetanus toxoid, diphtheria toxoid, Hepatitis B Surface Antigen (HBsAg), Hepatitis B core antigen (HBcAg), recombinant Protective Antigen or the L1 protein of the Human Papilloma Virus Virus Like Particle type 6, 11 or 16.

6. The conjugate according to any of claims 1-4 wherein the carrier protein is the outer membrane protein complex of *Neisseria meningitidis*.

7. A vaccine comprising a conjugate of any of claims 1-6, an adjuvant and a pharmaceutically acceptable excipient.

8. A vaccine comprising a conjugate of poly-D-gamma glutamic acid covalently linked to the outer membrane protein complex of *Neisseria meningitidis* by N-(epsilon-maleimidocaproic acid)hydrazide, an adjuvant and a pharmaceutically acceptable excipient.

9. A vaccine according to any of claims 7 and 8 further comprising at least one antigen selected from the group consisting of from *Haemophilus influenza*, hepatitis viruses A, B, or C, epitopes derived from the M2, hemagglutinin and neuraminidase proteins of Influenza virus types A or B, human papilloma virus, measles, mumps, rubella, varicella, rotavirus, *Streptococcus pneumonia* and *Staphylococcus aureus*.

10. A method of vaccinating a patient comprising administering an effective amount of a vaccine of any of claims 7-9.

5 11. A method of making a conjugate of poly-D-gamma glutamic acid and a carrier protein comprising activating the poly-D-gamma glutamic acid on a portion of its carboxylic acid side chains under non-aqueous conditions, introducing thiol reactive groups at the activated side chains and reacting the thiol reactive groups with a sulfhydryl containing carrier protein.

10 12. The method according to claim 11 comprising, providing purified poly-D-gamma glutamic acid as a hydrogen or tertbutylammonium salt, and removing water from the salt, and dissolving the salt in an organic solvent, and mixing the salt with N-(epsilon-maleimidocaproic acid)hydrazide, and adding an activating agent selected from the group consisting of N,N'-diisopropyl carbodiimide
15 and 4-(4,6-dimethoxy[1,3,5]triazin-2-yl)-4-methyl-morpholinium chloride, and diluting the reaction, and dialyzing the reaction, and adding thiolated outer membrane protein complex, and quenching residual thiols, and
20 isolating the conjugate.

13. A method of purifying poly-D-gamma glutamic acid comprising, dissolve partially purified extract containing poly-D-gamma glutamic acid in water, and mixing the solution with 0.004M sodium phosphate, pH 7.0 + 1M NaCl, and
25 load mixture on hydroxyapatite chromatography column, and washing out non-bound material with 0.004M sodium phosphate, pH 7.0 + 1M NaCl, and eluting poly-D-gamma glutamic acid with a linear gradient from 0 to 100% 0.4M sodium phosphate, pH 7.0 + 1M NaCl.

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